

## AMENDMENTS TO THE SPECIFICATION:

Amend Paragraph 0012 of the published application as follows:

Following the deposit of the micro-droplet on the selected sample support, the solvent can be evaporated from the micro-droplet under conditions that promote accumulation of the target analyte and the buffer or other compounds as spatially separated precipitates. It has been observed that deposits of biological polymers and oligomers including proteins, peptides, nucleotides, and other less soluble molecular analytes from a drop of liquid placed on a non-wetting substrate often accumulate in a circular ring formed during the evaporation process. This ring forming effect, sometimes referred to as the "coffee-ring" effect, localizes the deposited analyte and thus facilitates additional detection. Generally, the larger, less soluble components tend to precipitate near the edges of the deposit, while buffers and other more soluble compounds are distributed throughout the deposit region and more concentrated toward a central portion of the deposit. This analyte segregation method can also be used advantageously to segregate different analyte components in a mixture, such as compounds of different chemical composition and/or structure and thus facilitate the analysis of each separate component. The evaporation conditions required for optimal segregation can include temperature and other parameters that influence evaporation rate, such as the control of vapor phase convection of the solvent during the evaporation process. While the efficiency of this segregation process can in general depend on a number of variables, the process is generally applicable to biological compounds when using one of the previously

identified substrates and evaporating in ambient or desiccated air at normal room temperature. This method can also be applied at other lower or higher temperatures under various atmospheric conditions. Potential advantages of various conditions include higher evaporation speed (such as at higher temperature) or improved segregation of ~~different~~ different components (such as in higher solvent vapor pressure atmosphere). In some applications, high temperatures that might lead to degradation or denaturation of the biological compounds are to be avoided. This physical separation can be achieved by depositing a micro-droplet of solution, typically between 10 nl and 10  $\mu$ l on a selected substrate. The total time required for deposition and solvent evaporation at normal room temperature is typically about 10 minutes for  $\mu$ l depositions and only about 1 minute for nl depositions, which is roughly comparable to the time required for normal Raman signal collection.

Between Paragraph 0059 and the Heading "Description of Preferred Embodiments" of the published application, insert the following paragraphs:

Figure 33 is a schematic side elevational view of a molecular sample support in accordance with the present invention.

Figure 34 is a schematic side elevational view of another molecular sample support in accordance with the present invention.

Amend Paragraph 0060 of the published application as follows:

The analyte segregation and testing methods of the present invention generally requires a substantially planar solvophobic sample support 102 (Figure 33) or 104 (Figure 34) having an optically smooth surface 106, 108 desirably producing minimal interfering background signals such as luminescence and/or Raman scattering from the sample support alone. The sample supports 102, 104 are selected for their ability to diminish or restrict spreading of the sample and, preferably, to increase by surface tension the contact angle between the solvent of the sample and the surface. The sample supports 102, 104 generally comprise a substrate 110, 112 covered by a solvophobic enhancement layer 114, 116. Suitable substrates 110 (Figure 33) can include nominally flat metals such as gold, silver, platinum, titanium, aluminum, and alloys of these and other metals. The methods of the present invention can be practiced with substrates 110 consisting essentially of gold, which can be in the form of merely gold foil of about 0.1 mm thickness, or substrates 112 including a glass layer 118 coated with a layer 120 of about 10-100 nm of chromium and over coated with a layer 122 of about 10-100 nm of gold. The glass portion 118 of the substrate 112 can comprise a glass slide or cover slip, which exhibits a flat surface. A preferred sample support 102 can be constructed from a substrate 110 having a gold surface, such as previously described, further modified with a self-assembled organic monolayer forming the solvophobic enhancement layer 114. A self-assembled organic monolayer 114 particularly suitable for use on gold can be formed from alkyl chains with terminal thiol groups that bind to the gold surface. The solvophobic character of the alkyl chains can be manipulated by suitable selection of

organic residues. A further preferred substrate 110 is stainless steel coated with an about 50 nm layer of PTFE forming the solvophobic enhancement layer 114. The PTFE layer can be applied by spin coating at least one layer of a diluted PTFE resin material on the surface of the low background substrate. For example, a sample support having a solvophobic layer of less than about 50 microns can be made by spin coating a Teflon<sup>®</sup>. AF solution (Grade 400S1-100-1), available from DuPont (Wilmington, Del.) diluted with Fluorient FC-40, available from 3M Company (Minneapolis, Minn.) onto a gold layer that had been vacuum coated onto a glass support. The PTFE layer can be applied to a variety of substrates including optically transmissive as well as optically reflective surfaces.